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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/912,252	CROZE ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-24* is/are pending in the application.

4a) Of the above claim(s) *5 and 15-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-14 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed on 6/14/04 has been entered.

Claims 1 and 3-24 are pending in the present application.

This application contains claims 5, 15-21, drawn to an invention nonelected with traverse in the amendment filed on 7/17/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Amended claims 1, 3-4, 6-14 and new claims 22-24 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4 and 6-14 are rejected under 35 U.S.C. 112, first paragraph, because with respect to the elected invention the specification, while being enabling for:

A method of potentiating anti-growth effects of a type I interferon (IFN) on cells in a target cell population, said method comprises introducing **directly** into said cells an exogenous gene encoding an interferon receptor 2c receptor polypeptide (IFNAR2c) and then exposing the modified cells to a therapeutically effective amount of a type I IFN, and wherein the number of functional IFNAR2c receptor polypeptides on the surface of the modified cells is increased;

does not reasonably provide enablement for a method of potentiating anti-growth effects on a cells of a target cell population by introducing into said cells an exogenous gene encoding the IFNAR2c polypeptide by any route of delivery. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons already set forth in the previous Office Action mailed on 2/11/04 (pages 3-7).

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on 6/14/04 (pages 7-8) have been fully considered, but they are respectfully found to be unpersuasive.

With respect to the issue of delivery route, Applicants argue that that the introduction of a gene into a cell was routine and conventional on the date of application was filed. Applicants further argue that *in vivo* gene therapy has had success, perhaps not at the levels that might make it suitable for commercial use or to meet FDA approval which are not relevant to the statutory requirements. Moreover, Applicants cited the studies of Tada et al. (J. Clin. Invest. 108:83-95; 2001) and Cao et al. (Cancer gene therapy 8:497-505, 2001) to demonstrate that success has been achieved with gene therapy, and therefore one skilled in the art would reasonably conclude that transfection of cells with the IFNAR2c gene *in vivo* would be effective in the treatment of disease related to uncontrolled or abnormal growth. Applicants assert that the specification is

adequate to establish the patentability of the full scope of the claims, and the PTO has indicated that *in vivo* data is not necessary.

Applicant's arguments are respectfully found unpersuasive for the following reasons.

Firstly, although the introduction of a gene into a cell *in vitro* was routine and conventional on the date of application, targeting a gene into a target cell population *in vivo* to generate desired therapeutic effects (for this instance potentiating anti-growth effects of a type I interferon) was neither routine nor predictable as evidenced by the teachings of Dang et al., Verma & Somia, Romano et al. and Xu et al.

Secondly, it is noted that both Tada et al. and Cao et al. references are post-filing arts with respect to the effective filing date of the present application (7/26/2000). Moreover, none of these cited references teaches the delivery of a gene encoding IFNAR2c into a target cell population *in vivo* by any route of delivery to attain desired therapeutic effects. Examiner further notes that Cao et al. specifically teach intralesional delivery (or direct delivery) of an adenoviral vector encoding murine IFN-beta, while Tada et al. disclose intravenous delivery a recombinant adenovirus expressing human IFN-beta that targets liver due to the intrinsic property of the adenovirus vector in a nude mouse xenograft model of human colorectal cancer liver metastasis. Please note that the target cell population recited in the claims can be any cell population, and not necessarily limited to liver cells.

Thirdly, the courts have also stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application (27 USPQ2d 1662 *Ex parte Maizel.*).

Accordingly, upon analysis of the Wands factor as already set forth in the previous office, it would have require undue experimentation for a skilled artisan to make and use the instant broadly claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-4, 6-14 and new claims 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new ground of rejection necessitated by Applicants' amendment.**

In amended claim 1 and its dependent claims, it is unclear what is encompassed by the phrase "the anti-growth effects". Which anti-growth effects do Applicants claim? Clarification is requested because the metes and bounds of the claims are not clearly determined.

In new claims 22 and 24, the phrase "further comprising introducing an exogenous polynucleotide encoding the IFNAR2c polypeptide into cells in culture to form said modified cells" renders the claims indefinite. This is because it is unclear what is the relationship or connection between cells in culture with a target cell

population in claim 1 from which both claims 22 and 24 are dependent. Please note that the modified cells constitute a subset of and within the target cell population. It is unclear what exactly Applicants intend to claim. Clarification is requested because the metes and bounds of the claims are not clearly determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-4, 6 and 12-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Domanski et al. (J. Biol. Chem. 273:3144-3147, 1998) for the same reasons already set forth in the previous Office Action mailed on 2/11/04 (pages 8-9).

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on 6/14/04 (pages 9-10) have been fully considered, but they are respectfully found to be unpersuasive.

Applicants argue that antiproliferative and antiviral activities of IFN are not "inherently" as evidenced by the teachings of de la Maza et al., Khine and Lingwood and Fish et al., and therefore the anti-viral effects reported in Domanski et al. do not necessarily and inevitably lead to anti-growth effects. Additionally, Applicants argue

that the mixed system described by Domanski et al. does not provide clear data as to what interactions are being measured. Applicants further argue that the reference does not show "increasing the number of functional IFNAR2c receptor chains...:, and therefore the reference can not anticipate the presently claimed invention.

Applicants' arguments are respectfully found to be unpersuasive for the following reasons.

Firstly, none of the cited references of de la Maza et al., Khine and Lingwood, and Fish et al. teaches any cell transformed with an IFNAR2c gene, let alone mouse L-929 cells stably transformed with a recombinant plasmid expressing truncated IFNAR2c receptor chains. Moreover, de la Maza et al stated "In McCoy cells, there was a correlation among the antichlamydial antiviral, and antiproliferative activities of the different IFNs tested. In HeLa cells, however, the ability of a particular IFN subtype to inhibit Chlamydia infectivity did not **always** correlate with its inhibitory effects on encephalomyocarditis virus replication or with its antiproliferative activity" (see last two sentences of the abstract). Fish et al. showed clearly that human interferon subtypes have both anti-proliferative and antiviral activities on human cells (see Figures 1-3), although variations are observed among these activities depending on the interferon subtypes as well as target cells employed. Thus, there is no evidence suggesting or indicating that the method taught by Domanski et al. having the same method steps and the same materials (a cell and IFN concentrations within a therapeutically effective amount taught by this specification) would not result in antiproliferative effects for the transfected cells upon exposure to the applied various IFN concentrations.

Secondly, there is no reasonable explanation provided by Applicants to doubt that the transfected cells of Domanski et al. would not express functional exogenous IFNAR2c receptor chains.

Accordingly, claims 1, 3-4, 6 and 12-13 stand rejected under 35 U.S.C. 102(b) as being anticipated by Domanski et al. (J. Biol. Chem. 273:3144-3147, 1998) for the same reasons already set forth already set forth in the previous Office Action mailed on 2/11/04 (pages 8-9).

Claims 1, 3-4, 6, 12-13 and new claim 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Lutfalla et al. (EMBO J. 14:5100-5108, 1995). **This is a new ground of rejection necessitated by Applicants' addition of new claim 23, which is also applicable to claims 1, 3-4, 6 and 12-13.**

Lutfalla et al disclose a method in which human U5A cells were stably transfected with the pVADN1 vector expressing human IFNAR2-2 (U5A/ifnar2-2 cells), and the cells are exposed to various human recombinant type I IFN concentrations (3-30,000 IU/ml) in which 50% antiviral responses were observed (see the section titled "Complementation of the U5A mutant cell line by ifnar2-2", and particularly Table 1 on page 5105). Since the IFN concentrations utilized by Lutfalla et al. fall within a therapeutically effective amount of a type I IFN of the present invention (e.g., 50, 500 or 5000 IU/ml, see example 3 of the present specification), it is inherent that the method taught by Lutfalla et al. also results in anti-growth effects under the conditions disclosed.

Accordingly, Lutfalla et al. anticipate the instant claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Quang Nguyen, Ph.D.